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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

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Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> s ruthenium and p-cymene and [anticancer or antitumor]
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> s ruthenium and p-cymene
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                1.68       1.68

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=> s ruthenium and (anticancer or antitumor) and (p-cymene)
         96437 RUTHENIUM
            23 RUTHENIUMS
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         96437 RUTHENIUM
                 (RUTHENIUM OR RUTHENIUMS)
         40236 ANTICANCER
            52 ANTICANCERS
         40259 ANTICANCER
                 (ANTICANCER OR ANTICANCERS)
        224927 ANTITUMOR
           388 ANTITUMORS
        224944 ANTITUMOR
                 (ANTITUMOR OR ANTITUMORS)
       2533852 P
         12628 CYMENE
           273 CYMENES
         12680 CYMENE
                 (CYMENE OR CYMENES)
         10884 P-CYMENE
                 (P(W)CYMENE)
L1          28 RUTHENIUM AND (ANTICANCER OR ANTITUMOR) AND (P-CYMENE)

=> d scan

L1    28 ANSWERS   CAPLUS  COPYRIGHT 2007 ACS on STN
CC    29-13 (Organometallic and Organometalloidal Compounds)
      Section cross-reference(s): 1, 75
TI    In Vitro Evaluation of Rhodium and Osmium RAPTA Analogues: The Case for
      Organometallic Anticancer Drugs Not Based on Ruthenium
ST    rhodium half sandwich complex substitution pta; crystal structure rhodium
      half sandwich pta complex prepn; mol structure rhodium half sandwich pta
      complex prepn; cytotoxicity RAPTA osmium analog rhodium half sandwich pta
      complex; antitumor rhodium half sandwich pta complex evaluation
      RAPTA complex
IT    Bond length
         (carbon-metal, rhodium-cyclopentadienyl (centroid); preparation and
         structures of half-sandwich rhodium pta complexes and their in vitro
         evaluation as organometallic anticancer drugs in comparison
         with RAPTA-C and osmium RAPTA analog)
IT    Lung, neoplasm
      Mammary gland, neoplasm
         (carcinoma; preparation and structures of half-sandwich rhodium pta
         complexes and their in vitro evaluation as organometallic
         anticancer drugs in comparison with RAPTA-C and osmium RAPTA
         analog)
IT    Intestine, neoplasm
         (colon, carcinoma; preparation and structures of half-sandwich rhodium pta
         complexes and their in vitro evaluation as organometallic
         anticancer drugs in comparison with RAPTA-C and osmium RAPTA
         analog)
IT    Carcinoma
         (colon; preparation and structures of half-sandwich rhodium pta complexes
         and their in vitro evaluation as organometallic anticancer
         drugs in comparison with RAPTA-C and osmium RAPTA analog)
IT    Bond length
         (coordinate, phosphorus-rhodium; preparation and structures of half-sandwich
         rhodium pta complexes and their in vitro evaluation as organometallic
         anticancer drugs in comparison with RAPTA-C and osmium RAPTA
         analog)
IT    Sandwich compounds
      RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN
      (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT
      (Reactant or reagent)
         (half-sandwich, rhodium, ruthenium and osmium; preparation and
         structures of half-sandwich rhodium pta complexes and their in vitro
         evaluation as organometallic anticancer drugs in comparison
         with RAPTA-C and osmium RAPTA analog)
IT    Carcinoma
```

(mammary; preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT Crystal structure
Molecular structure
(of half-sandwich rhodium pta complexes)

IT Antitumor agents
Human
Substitution reaction, coordinative
Through-space interaction
(preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT Carcinoma
(pulmonary; preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT 908356-25-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(crystal structure; preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT 908356-29-6P 908356-32-1P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(crystal structure; preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT 908356-26-3P 908356-31-0P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(mol. structure; preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT 852172-35-1
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT 372948-28-2
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT 908356-27-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT 908356-33-2P
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT 143-66-8, Sodium tetraphenylborate 12354-85-7 32627-01-3, Dicarbonyl(η5-pentamethylcyclopentadienyl)rhodium 33677-50-8, (η5-Cyclopentadienyl)bis(triphenylphosphine)rhodium 53597-69-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and structures of half-sandwich rhodium pta complexes and their

in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

IT 908356-28-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and structures of half-sandwich rhodium pta complexes and their in vitro evaluation as organometallic anticancer drugs in comparison with RAPTA-C and osmium RAPTA analog)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):none

=> d l1 1-28 abs ibib hitstr

L1 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Relatively little is known about the kinetics or the pharmacol. potential of organometallic complexes of osmium compared to its lighter congeners, iron and ruthenium. We report the synthesis of seven new complexes, [(η6-arene)Os(NN)Cl]+, containing different bidentate nitrogen (N,N) chelators, and a dichlorido complex, [(η6-arene)Os(N)Cl2]. The X-ray crystal structures of seven complexes are reported: [(η6-bip)Os(en)Cl]PF6 (1PF6), [(η6-THA)Os(en)Cl]BF4 (2BF4), [(η6-p-cym)Os(phen)Cl]PF6 (5PF6), [(η6-bip)Os(dppz)Cl]PF6 (6PF6), [(η6-bip)Os(azpy-NMe2)Cl]PF6 (7PF6), [(η6-p-cym)Os(azpy-NMe2)Cl]PF6 (8PF6), and [(η6-bip)Os(NCCH3-N)Cl2] (9), where THA = tetrahydroanthracene, en = ethylenediamine, p-cym = p-cymene, phen = phenanthroline, bip = biphenyl, dppz = [3,2-a:2',3'-c]phenazine and azpy-NMe2 = 4-(2-pyridylazo)-N,N-dimethylaniline. The chelating ligand was found to play a crucial role in enhancing aqueous stability. The rates of hydrolysis at acidic pH* decreased when the primary amine N-donors (NN = en, t1/2 = 0.6 h at 318 K) are replaced with π-accepting pyridine groups (e.g., NN = phen, t1/2 = 9.5 h at 318 K). The OsII complexes hydrolyze up to 100 times more slowly than their RuII analogs. The pK*a of the aqua adducts decreased with a similar trend (pK*a = 6.3 and 5.8 for en and phen adducts, resp.). [(η6-bip)Os(en)Cl]PF6/BF4 (1PF6/BF4) and [(η6-THA)Os(en)Cl]BF4 (2BF4) were cytotoxic toward both the human A549 lung and A2780 ovarian cancer cell lines, with IC50 values of 6-10 μM, comparable to the anticancer drug carboplatin. 1BF4 binds to both the N7 and phosphate of 5'-GMP (ratio of 2:1). The formation constant for the 9-ethylguanine (9EtG) adduct [(η6-bip)M(en)(9EtG)]2+ was lower for OsII (log K = 3.13) than RuII (log K = 4.78), although the OsII adduct showed some kinetic stability. DNA intercalation of the dppz ligand in 6PF6 may play a role in its cytotoxicity. This work demonstrates that the nature of the chelating ligand can play a crucial role in tuning the chemical and biol. properties of [(η6-arene)Os(NN)Cl]+ complexes.

ACCESSION NUMBER: 2007:427928 CAPLUS
TITLE: Chloro Half-Sandwich Osmium(II) Complexes: Influence of Chelated N,N-Ligands on Hydrolysis, Guanine Binding, and Cytotoxicity
AUTHOR(S): Peacock, Anna F. A.; Habtemariam, Abraha; Moggach, Stephen A.; Prescimone, Alessandro; Parsons, Simon; Sadler, Peter J.
CORPORATE SOURCE: School of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: Inorganic Chemistry (Washington, DC, United States) (2007), 46(10), 4049-4059
CODEN: INOCAJ; ISSN: 0020-1669
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Organometallic ruthenium(II) complexes of the general formula [Ru(η6- p-cymene)Cl2(L)] and [Ru(η6- p

-cymene)Cl(L)2][BPh4] with modified phenoxazine- and anthracene-based multidrug resistance (MDR) modulator ligands (L) have been synthesized, spectroscopically characterized, and evaluated in vitro for their cytotoxic and MDR reverting properties in comparison with the free ligands. For an anthracene-based ligand, coordination to a ruthenium(II) arene fragment led to significant improvement of cytotoxicity as well as Pgp inhibition activity. A similar, but weaker effect was also observed when using a benzimidazole-phenoxazine derivative as Pgp inhibitor. The most active compound in terms of both Pgp inhibition and cytotoxicity is [Ru(η6- p-cymene)Cl2(L)], where L is an anthracene-based ligand. Studies show that it induces cell death via inhibition of DNA synthesis. Moreover, because the complex is fluorescent, its uptake in cells was studied, and relative to the free anthracene-based ligand, uptake of the complex is accelerated and accumulation of the complex in the cell nucleus is observed

ACCESSION NUMBER: 2007:394251 CAPLUS
TITLE: Development of Ruthenium Antitumor Drugs that Overcome Multidrug Resistance Mechanisms
AUTHOR(S): Vock, Carsten A.; Ang, Wee Han; Scolaro, Claudine; Phillips, Andrew D.; Lagopoulos, Lucienne; Juillerat-Jeanneret, Lucienne; Sava, Gianni; Scopelliti, Rosario; Dyson, Paul J.
CORPORATE SOURCE: Institut des Sciences et Ingenierie Chimiques, Ecole Polytechnique Federale de Lausanne (EPFL), Lausanne, CH-1015, Switz.
SOURCE: Journal of Medicinal Chemistry (2007), 50(9), 2166-2175
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB D. functional calcns. show that aquation of [Os(η6-are-ne)(XY)Cl]n+ complexes is more facile for complexes in which XY = an anionic O,O-chelated ligand compared to a neutral N,N-chelated ligand, and the mechanism more dissociative in character. The O,O-chelated XY = maltolato (mal) [M(η6-p-cym)(mal)Cl] complexes, in which p-cym = p-cymene, M = OsII (1) and RuII (2), were synthesized and the X-ray crystal structures of 1 and 2·2H2O determined Their hydrolysis rates were rapid (too fast to follow by NMR spectroscopy). The aqua adduct of the OsII complex 1 was 1.6 pKa units more acidic than that of the RuII complex 2. Dynamic NMR studies suggested that O,O-chelate ring opening occurs on a millisecond timescale in coordinating proton-donor solvents, and loss of chelated mal in aqueoussoln. led to the formation of the hydroxo-bridged dimers [(η6-p-cym)M(μ-OH)3M(η6-p-cym)]+. The proportion of this dimer in solns. of the OsII complex 1 increased with dilution and it predominated at micromolar concns., even in the presence of 0.1 M NaCl (conditions close to those used for cytotoxicity testing). Although 9-ethylguanine (9-EtG) binds rapidly to OsII in 1 and more strongly (log K = 4.4) than to RuII in 2 (log K = 3.9), the OsII adduct [Os(η6-p-cym)(mal)-(9EtG)]+ was unstable with respect to formation fo the hydroxo-bridged dimer at micromolar concns. Such insights into the aqueous solution chemical of metal-arene complexes under biol. relevant conditions will aid the rational design of organometallic anticancer agents.

ACCESSION NUMBER: 2007:365079 CAPLUS
TITLE: Osmium(II) and ruthenium(II) arene maltolato complexes: rapid hydrolysis and nucleobase binding
AUTHOR(S): Peacock, Anna F. A.; Melchart, Michael; Deeth, Robert J.; Habtemariam, Abraha; Parsons, Simon; Sadler, Peter

J.
CORPORATE SOURCE: School of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: Chemistry--A European Journal (2007), 13(9), 2601-2613
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB We rationalize the chemoselectivity of the monofunctional ruthenium anticancer compound [(η6-arene)Ru(II)(en)(OH2)]2+ (en=ethylenediamine; arene=benzene 1, p-cymene 2) toward guanine, using static DFT (BP86) and MP2 calcns. together with Car-Parrinello mol. dynamics. The calculated binding energies for the three investigated nucleobases (G, A, C) decreases in the order G(N7) » C(O2) .apprx. C(N3) > A(N7) > G(O6) > OH2. The G(N7) complex is the most stable product due to a hydrogen bond of its O6 with one of the H2N-amine groups of en, while the corresponding NH2-H2N(en) interaction in the adenine complex is repulsive. A very low rotational barrier of 0.17 kcal/mol (BP86) and 0.64 kcal/mol (MP2) was calculated for the arene rotation in [(η6-C6H6)Ru(en)(Cl)]+ (3) allowing complexes containing arenes with bulky side chains like p-cymene to minimize steric interactions with, e.g., DNA by simple arene rotation. All [(η6-arene)Ru(en)(L)]2+ compds. exist in two stable conformers obtained for different diamine dihedral angle (NCCN) orientation, which, in the case of asym. ligands L, differ by up to .apprx.2.8 kcal/mol. Car-Parrinello dynamics reveal a chelating transition state for the interconversion between N7 and O6 binding of guanine to [(η6-arene)Ru(en)]2+.
ACCESSION NUMBER: 2007:349580 CAPLUS
TITLE: Structural and Energetic Properties of Organometallic Ruthenium(II) Diamine Anticancer Compounds and Their Interaction with Nucleobases
AUTHOR(S): Gossens, Christian; Tavernelli, Ivano; Rothlisberger, Ursula
CORPORATE SOURCE: Institut des Sciences et Ingenierie Chimiques, Ecole Polytechnique Federale de Lausanne (EPFL), Lausanne, CH-1015, Switz.
SOURCE: Journal of Chemical Theory and Computation (2007), 3(3), 1212-1222
CODEN: JCTCCE; ISSN: 1549-9618
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB On page 10888, the text should read: "Azpy displays a weak n→π* (forbidden) transition at 445 nm, and while this transition was not observed for the other ligands, it may be masked by the intense π→π*transitions.". On page 10888 the text should read: "Upon deprotonation of azpy-OH, the π→π*transitions shift from 246 and 358 nm to 268 and 435 nm.". On page 10889, the caption of Figure 6 is incorrect; the correct caption is given.
ACCESSION NUMBER: 2007:82214 CAPLUS
TITLE: Phenylazo-pyridine and Phenylazo-pyrazole Chlorido Ruthenium(II) Arene Complexes: Arene Loss, Aquation, and Cancer Cell Cytotoxicity. [Erratum to document cited in CA146:206434]
AUTHOR(S): Dougan, Sarah J.; Melchart, Michael; Habtemariam, Abraha; Parsons, Simon; Sadler, Peter J.

CORPORATE SOURCE: School of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: Inorganic Chemistry (2007), 46(4), 1508
CODEN: INOCAJ; ISSN: 0020-1669
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Errata
LANGUAGE: English
IT INDEXING IN PROGRESS

L1 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Ru(II) η6-arene complexes containing p-cymene (p-cym), tetrahydronaphthalene (thn), benzene (bz), or biphenyl (bip), as the arene, phenylazopyridine derivs. (C5H4NN:NC6H4R-4; R = H (azpy), OH (azpy-OH), NMe2 (azpy-NMe2)) or a phenylazopyrazole derivative (NHC3H2NN:NC6H4NMe2-4 (azpyz-NMe2)) as N,N-chelating ligands and chloride as a ligand were synthesized (1-16). The complexes are all intensely colored due to metal-to-ligand charge-transfer Ru 4d6-π* and intraligand π → π* transitions (ε = 5000-63,700 M-1 cm-1) occurring in the visible region. In the crystal structures of [(η6-p-cym)Ru(azpy)Cl]PF6 (1), [(η6-p-cym)Ru(azpy-NMe2)Cl]PF6 (5), and [(η6-bip)Ru(azpy)Cl]PF6 (4), the relatively long Ru-N(azo) and Ru-(arene-centroid) distances suggest that phenylazopyridine and arene ligands can act as competitive π-acceptors toward Ru(II) 4d6 electrons. The pKa* values of the pyridine nitrogens of the ligands are low (azpy 2.47, azpy-OH 3.06 and azpy-NMe2 4.60), suggesting that they are weak σ-donors. This, together with their π-acceptor behavior, serves to increase the pos. charge on Ru, and together with the π-acidic η6-arene, partially accounts for the slow decomposition of the complexes via hydrolysis and/or arene loss (t1/2 = 9-21 h for azopyridine complexes, 310 K). The pKa* of the coordinated H2O in [(η6-p-cym)Ru(azpyz-NMe2)OH2]2+ (13A) is 4.60, consistent with the increased acidity of the Ru center upon coordination to the azo ligand. None of the azpy complexes were cytotoxic toward A2780 human ovarian or A549 human lung cancer cells, but several of the azpy-NMe2, azpy-OH, and azpyz-NMe2 complexes were active (IC50 values 18-88 μM).
ACCESSION NUMBER: 2006:1294354 CAPLUS
DOCUMENT NUMBER: 146:206434
TITLE: Phenylazo-pyridine and Phenylazo-pyrazole Chlorido Ruthenium(II) Arene Complexes: Arene Loss, Aquation, and Cancer Cell Cytotoxicity
AUTHOR(S): Dougan, Sarah J.; Melchart, Michael; Habtemariam, Abraha; Parsons, Simon; Sadler, Peter J.
CORPORATE SOURCE: School of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: Inorganic Chemistry (2006), 45(26), 10882-10894
CODEN: INOCAJ; ISSN: 0020-1669
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Ruthenium arene complexes containing bidentate diamine, amino acid and diketonate chelate ligands were prepared by a variety of appropriate procedures and examined for cytostatic activity against human cancer cells. Organometallic Ru(II) complexes [(η6-arene)Ru(XY)Cl]Z, where XY is an N,N- (diamine), N,O- (e.g., amino acidate), or O,O- (e.g., β-diketonate) chelating ligand, the arene ranges from benzene derivs. to fused polycyclic hydrocarbons, and Z is usually PF6, were prepared by direct or reduction-assisted complexation of arenes, substitution of cycloalkadiene or arene ligands with subsequent complexation of bidentate XY-ligands. The x-ray structures of 13 complexes are reported. All have the characteristic "piano-stool" geometry. The structure-activity relationships was evaluated for cytotoxicity of the prepared complexes

against human cancer cells. The complexes most active toward A2780 human ovarian cancer cells contained XY = ethylenediamine (en) and extended polycyclic arenes. Complexes with polar substituents on the arene or XY = bipyridyl derivs. exhibited reduced activity. The activity of the O,O-chelated complexes depended strongly on the substituents and on the arene. For arene = p-cymene, XY = amino acidate complexes were inactive. Complexes were not cross-resistant with cisplatin, and cross-resistance to Adriamycin was circumvented by replacing XY = en with 1,2-phenylenediamine. Some complexes were also active against colon, pancreatic, and lung cancer cells.

ACCESSION NUMBER: 2006:1079231 CAPLUS
DOCUMENT NUMBER: 146:27919
TITLE: Structure-Activity Relationships for Cytotoxic Ruthenium(II) Arene Complexes Containing N,N-, N,O-, and O,O-Chelating Ligands
AUTHOR(S): Habtemariam, Abraha; Melchart, Michael; Fernandez, Rafael; Parsons, Simon; Oswald, Iain D. H.; Parkin, Andrew; Fabbiani, Francesca P. A.; Davidson, James E.; Dawson, Alice; Aird, Rhona E.; Jodrell, Duncan I.; Sadler, Peter J.
CORPORATE SOURCE: School of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: Journal of Medicinal Chemistry (2006), 49(23), 6858-6868
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:27919
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Reaction of [Ru(η6- p-cymene)Cl2]2 with K[oxine] in CH2Cl2 gave Ru(η6- p-cymene)(oxine)Cl which on sequential treatment with AgCF3SO3 in THF and pyrazole gave title compound, [Ru(η6- p-cymene)(oxine)(κ1-Hpz)]CF3SO3 (3). The crystal structure and antitumor activity of 3 was determined

ACCESSION NUMBER: 2006:957944 CAPLUS
DOCUMENT NUMBER: 146:358959
TITLE: Ruthenium(II)-arene complex with heterocyclic ligands as prospective antitumor agent
AUTHOR(S): John, Roland O.; Arion, Vladimir B.; Jakupec, Michael A.; Keppler, Bernhard K.
CORPORATE SOURCE: Institute of Inorganic Chemistry, University of Vienna, Vienna, 1090, Austria
SOURCE: Metal Ions in Biology and Medicine (2006), 9, 40-45
CODEN: MIBMCT; ISSN: 1257-2535
PUBLISHER: John Libbey Eurotext
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:358959
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB We have studied the interaction of the organometallic anticancer ruthenium(II) complexes [(η6- p-cymene)Ru(en)Cl][PF6] (1) and [(η6-biphenyl)Ru(en)Cl][PF6] (2) (en=ethylenediamine) with the single-stranded (ss) DNA hexamer d(CGGCCG) (I) and the duplex d(CGGCCG)2 (II) by HPLC, ESI-MS, and one- and two-dimensional 1H and 15N NMR spectroscopy. For ss-DNA, all three G's are readily ruthenated with [(η6-arene)-Ru(en)]2+, but for duplex DNA there is preferential ruthenation of G3 and G6, and no binding to G2 was

detected. For monoruthenated duplexes, N7 ruthenation of G is accompanied by strong hydrogen bonding between G-O6 and en-NH for the p-cymene adducts. Intercalation of the non-coordinated Ph ring between G3 and C4 or G6 and C5 was detected in the biphenyl adducts of mono- and diruthenated duplexes, together with weakening of the G-O6···NH-en hydrogen bonding. The arene ligand plays a major role in distorting the duplex either through steric interactions (p-cymene) or through intercalation (biphenyl).

ACCESSION NUMBER: 2006:829509 CAPLUS
DOCUMENT NUMBER: 145:433516
TITLE: Ruthenation of duplex and single-stranded d(CGGCCG) by organometallic anticancer complexes
AUTHOR(S): Liu, L, Hong-Ke; Wang, Fuyi; Parkinson, John A.; Bella, Juraj; Sadler, Peter J.
CORPORATE SOURCE: School of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: Chemistry--A European Journal (2006), 12(23), 6151-6165
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Ruthenium arene half-sandwich imidazole, benzimidazole, pyridine and morpholine complexes were prepared and evaluated for their cytotoxicity against tumor cells. Ten complexes [Ru(η6-arene)Cl2(L)], [Ru(η6-arene)Cl(L)2][X], and [Ru(η6-arene)(L)3][X]2 (η6-arene = benzene, p-cymene; L = imidazole-N3, benzimidazole-N3, N-methylimidazole-N3, N-butylimidazole-N3, N-vinylimidazole-N3, N-benzoylimidazole-N3, pyridine, morpholine-N; X = Cl, BF4, BPh4) were prepared by reaction of [(arene)2Ru2(μ-Cl)2Cl2] with the corresponding ligands; the complexes were spectroscopically characterized. The structures of five representative compds. were confirmed by single-crystal x-ray crystallog. anal. All the new compds. were assessed by in vitro screening cytotoxicity assays against murine adenocarcinoma cell lines. The new compds. show essentially the same order of cytotoxicity as the known 1,3,5-triaza-7-phosphaadamantane ruthenium complex (RAPTA). Several of the compds. were selective toward cancer cells in that they were less (or not) cytotoxic toward non-tumorigenic cells that are used to model healthy human cells. Thus, two of the compds., [Ru(η6- p-cymene)Cl(N-vinylimidazole)2][Cl] and [Ru(η6-benzene)(N-methylimidazole)3][BF4]2 have been selected for a more detailed in vivo evaluation.

ACCESSION NUMBER: 2006:784692 CAPLUS
DOCUMENT NUMBER: 145:377456
TITLE: Synthesis, Characterization, and in Vitro Evaluation of Novel Ruthenium(II) η6-Arene Imidazole Complexes
AUTHOR(S): Vock, Carsten A.; Scolaro, Claudine; Phillips, Andrew D.; Scopelliti, Rosario; Sava, Gianni; Dyson, Paul J.
CORPORATE SOURCE: Institut des Sciences et Ingenierie Chimiques, Ecole Polytechnique Federale de Lausanne (EPFL), Lausanne, CH-1015, Switz.
SOURCE: Journal of Medicinal Chemistry (2006), 49(18), 5552-5561
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:377456

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

AB Reaction of the dimer [(η5-C5Me5)RhCl(μ2-Cl)]2 with 2 or 4 equiv of the water-soluble phosphine 1,3,5-triaza-7-phosphatricyclo[3.3.1.1]decane (pta) affords [Rh(η5-C5Me5)(pta)Cl2] in 73% and [Rh(η5-C5Me5)(pta)2Cl]Cl in 77% yields, resp. Both complexes have been characterized in solution by NMR spectroscopy and in the solid state by single-crystal x-ray diffraction, the latter as the chloride and BPh4- salts. In addition, the rhodium(I) complexes [Rh(η5-C5Me5)(CO)(pta)] (60% yield) and [Rh(η5-C5H5)(pta)2] (30% yield) have been prepared from [Rh(η5-C5Me5)(CO)2] and [Rh(η5-C5H5)(PPh3)2], resp., by reaction with pta. An in vitro evaluation of these compds., together with [Os(η6-C10H14)(pta)Cl2] (C10H14 = p-cymene) and the well-characterized antimetastasis drug [Ru(η6-C10H14)(pta)Cl2], RAPTA-C, was undertaken using HT29 colon carcinoma, A549 lung carcinoma, and T47D breast carcinoma cells. In the HT29 cell line, the two nearest congeners to [Ru(η6-C10H14)(pta)Cl2], viz., [Rh(η5-C5Me5)(pta)Cl2] and [Os(η6-C10H14)(pta)Cl2], demonstrated very similar cytotoxicity profiles. [Rh(η5-C5Me5)(pta)Cl2] proved significantly more cytotoxic in A549 cells and [Rh(η5-C5Me5)(pta)2Cl]Cl 3-fold more cytotoxic in T47D cells, both relative to RAPTA-C. These data suggest that the development of organometallic anticancer drugs based on the neighboring elements to ruthenium should not be overlooked.

ACCESSION NUMBER: 2006:672933 CAPLUS
DOCUMENT NUMBER: 145:293173
TITLE: In Vitro Evaluation of Rhodium and Osmium RAPTA Analogues: The Case for Organometallic Anticancer Drugs Not Based on Ruthenium
AUTHOR(S): Dorcier, Antoine; Ang, Wee Han; Bolano, Sandra; Gonsalvi, Luca; Juillerat-Jeannerat, Lucienne; Laurenczy, Gabor; Peruzzini, Maurizio; Phillips, Andrew D.; Zanobini, Fabrizio; Dyson, Paul J.
CORPORATE SOURCE: Institut des Sciences et Ingenierie Chimiques, Ecole Polytechnique Federale de Lausanne (EPFL), Lausanne, CH-1015, Switz.
SOURCE: Organometallics (2006), 25(17), 4090-4096
CODEN: ORGND7; ISSN: 0276-7333
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:293173
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

AB Optimization of the design of half-sandwich organometallic RuII arene complexes as anticancer agents depends on control of ligand exchange reactions. The aqueous chemical of complexes containing O,O-chelate rings are studied. The presence of the four-membered O,O-chelate ring from acetate (AcO) in [(η6- p-cymene)Ru(AcO)Cl] was confirmed by x-ray crystallog., but in solution the acetate ligand was labile and the hydroxo-bridged dimer [((η6- p-cymene)Ru)2(μ-OH)3]+ readily formed. The dimer was relatively unreactive towards 9-Et guanine. The tropolonato (trop) complex [(η6- p -cymene)Ru(trop)Cl] was stable in aqueous media and the x-ray crystal structure of the aqua adduct [(η6- p-cymene)Ru(trop)(H2O)]CF3SO3, containing a five-membered O,O-chelate ring from trop, was determined [(η6- p-cymene)Ru(trop)Cl] reacted with guanosine to form N7 adducts and with adenosine to form both N7 and N1 adducts. Competitive reactions with guanosine and adenosine gave rise to guanosine:adenosine adducts in a ca. 1.3:1 mol ratio.

ACCESSION NUMBER: 2006:484913 CAPLUS
DOCUMENT NUMBER: 145:167392
TITLE: Ruthenium(II) arene complexes containing four- and five-membered monoanionic O,O-chelate rings
AUTHOR(S): Melchart, Michael; Habtemariam, Abraha; Parsons, Simon; Moggach, Stephen A.; Sadler, Peter J.
CORPORATE SOURCE: School of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: Inorganica Chimica Acta (2006), 359(9), 3020-3028
CODEN: ICHAA3; ISSN: 0020-1693
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:167392
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Ruthenium(II) arene anticancer complexes [(η 6-arene)Ru(en)Cl]PF6 (arene is hexamethylbenzene, p-cymene, indan; en is ethylenediamine) can catalyze regioselective reduction of NAD+ by formate in water to form 1,4-NADH, at pD 7.2, 37°, and in the presence of air. The catalytic activity is markedly dependent on the arene, with the hexamethylbenzene (hmb) complex showing the highest activity. For [(η 6-hmb)Ru(en)Cl]PF6, the rate of reaction is independent of NAD+ concentration and shows saturation kinetics with respect to formate concentration A Km value of 58 mM and a turnover frequency at saturation of 1.46 h-1 were observed Removal of chloride and performing the reaction under argon led to higher reaction rates. Lung cancer cells (A549) were found to be remarkably tolerant to formate even at millimolar concns. The possibility of using ruthenium arene complexes coadministered with formate as catalytic drugs is discussed.
ACCESSION NUMBER: 2006:431631 CAPLUS
DOCUMENT NUMBER: 145:119261
TITLE: Catalysis of regioselective reduction of NAD+ by ruthenium(II) arene complexes under biologically relevant conditions
AUTHOR(S): Yan, Yaw Kai; Melchart, Michael; Habtemariam, Abraha; Peacock, Anna F. A.; Sadler, Peter J.
CORPORATE SOURCE: School of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: JBIC, Journal of Biological Inorganic Chemistry (2006), 11(4), 483-488
CODEN: JJBCFA; ISSN: 0949-8257
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB The OsII arene ethylenediamine (en) complexes [(η6-biphenyl)Os(en)Cl][Z], Z = BPh4 (4) and BF4 (5), are inactive toward A2780 ovarian cancer cells despite 4 being isostructural with an active RuII analog, 4R. Hydrolysis of 5 occurred 40 times more slowly than 4R. The aqua adduct 5A has a low pKa (6.3) compared to that of [(η6-biphenyl)Ru(en)(OH2)]2+ (7.7) and is therefore largely in the hydroxo form at physiol. pH. The rate and extent of reaction of 5 with 9-ethylguanine were also less than those of 4R. The authors replaced the neutral en ligand by anionic acetylacetonate (acac). The complexes [(η6-arene)Os(acac)Cl], arene = biphenyl (6), benzene (7), and p-cymene (8), adopt piano-stool structures similar to those of the RuII analogs and form weak dimers through intermol. (arene)C-H···O(acac) H-bonds. Remarkably, these OsII

acac complexes undergo rapid hydrolysis to produce not only the aqua adduct, [(η6-arene)Os(acac)(OH2)]+, but also the hydroxo-bridged dimer, [(η6-arene)Os(μ2-OH)3Os(η6-arene)]+. The pKa values for the aqua adducts 6A, 7A, and 8A (7.1, 7.3, and 7.6, resp.) are lower than that for [(η6- p-cymene)Ru(acac)(OH2)]+ (9.4). Complex 8A rapidly forms adducts with 9-ethylguanine and adenosine, but not with cytidine or thymidine. Despite their reactivity toward nucleobases, complexes 6-8 were inactive toward A549 lung cancer cells. This is attributable to rapid hydrolysis and formation of unreactive hydroxo-bridged dimers which, surprisingly, were the only species present in aqueous solution at biol. relevant concns. Hence, the choice of chelating ligand in OsII (and RuII) arene complexes can have a dramatic effect on hydrolysis behavior and nucleobase binding and provides a means of tuning the reactivity and the potential for discovery of anticancer complexes.

ACCESSION NUMBER: 2006:38977 CAPLUS
DOCUMENT NUMBER: 144:285767
TITLE: Tuning the Reactivity of Osmium(II) and Ruthenium(II) Arene Complexes under Physiological Conditions
AUTHOR(S): Peacock, Anna F. A.; Habtemariam, Abraha; Fernandez, Rafael; Walland, Victoria; Fabbiani, Francesca P. A.; Parsons, Simon; Aird, Rhona E.; Jodrell, Duncan I.; Sadler, Peter J.
CORPORATE SOURCE: School of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: Journal of the American Chemical Society (2006), 128(5), 1739-1748
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:285767
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB The antitumor activity of the organometallic ruthenium (II)-arene complexes, RuCl2(η6-arene)(PTA), (arene = p-cymene, toluene, benzene, benzo-15-crown-5, 1-ethylbenzene-2,3-dimethylimidazolium tetrafluoroborate, Et benzoate, hexamethylbenzene; PTA = 1,3,5-triaza-7-phosphaadamantane), abbreviated RAPTA, has been evaluated. In vitro biol. expts. demonstrate that these compds. are active toward the TS/A mouse adenocarcinoma cancer cell line whereas cytotoxicity on the HBL-100 human mammary (nontumor) cell line was not observed at concns. up to 0.3 mM, which indicates selectivity of these ruthenium(II)-arene complexes to cancer cells. Analogs of the RAPTA compds., in which the PTA ligand is methylated, have also been prepared, and these prove to be cytotoxic toward both cell lines. RAPTA-C and the benzene analog RAPTA-B were selected for in vivo expts. to evaluate their anticancer and antimetastatic activity. The results show that these complexes can reduce the growth of lung metastases in CBA mice bearing the MCa mammary carcinoma in the absence of a corresponding action at the site of primary tumor growth. Pharmacokinetic studies of RAPTA-C indicate that ruthenium is rapidly eliminated from the organs and the bloodstream.

ACCESSION NUMBER: 2005:434823 CAPLUS
DOCUMENT NUMBER: 143:125821
TITLE: In Vitro and in Vivo Evaluation of Ruthenium (II)-Arene PTA Complexes
AUTHOR(S): Scolaro, Claudine; Bergamo, Alberta; Brescacin, Laura; Delfino, Riccarda; Cocchietto, Moreno; Laurenczy, Gabor; Geldbach, Tilmann J.; Sava, Gianni; Dyson, Paul J.
CORPORATE SOURCE: Institut des Sciences et Ingenierie Chimiques, Ecole

Polytechnique Federale de Lausanne (EPFL), Lausanne, CH-1015, Switz.
SOURCE: Journal of Medicinal Chemistry (2005), 48(12), 4161-4171
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:125821
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Organometallic Ru(II)-arene complexes are currently attracting increasing interest as anticancer compds. with the potential to overcome drawbacks of traditional drugs like cisplatin with respect to resistance, selectivity, and toxicity. Rational design of new potential pharmaceutical compds. requires a detailed understanding of structure-property relations at an atomic level. In vacuo d. functional theory (DFT) calcns., classical MD, and mixed QM/MM Car-Parrinello MD explicit solvent simulations to rationalize the binding mode of two series of anticancer Ru(II) arene complexes to double-stranded DNA (dsDNA) was performed. Binding energies between the metal centers and the surrounding ligands as well as proton affinities were calculated using DFT. Results support a pH-dependent mechanism for the activity of the RAPTA [Ru(η6-arene)X2(pta)] (pta = 1,3,5-triaza-7-phosphatricyclo[3.3.1.1]decane) compds. Adducts of the bifunctional RAPTA and the monofunctional [Ru(η6- p-cymene)Xen]+ series of compds. with the DNA sequence d(CCTCTG*G*TCTCC)/d(GGAGACCAGAGG), where G* are guanosine bases that bind to the Ru compds. through their N(7) atom, were studied. The resulting binding sites were characterized in QM/MM mol. dynamics simulations showing that DNA can easily adapt to accommodate the Ru compds.
ACCESSION NUMBER: 2005:386195 CAPLUS
DOCUMENT NUMBER: 144:254216
TITLE: Rational design of organo-ruthenium anticancer compounds
AUTHOR(S): Gossens, Christian; Tavernelli, Ivano; Rothlisberger, Ursula
CORPORATE SOURCE: Laboratory of Computational Chemistry and Biochemistry, Institut des Sciences et Ingenierie Chimiques, Ecole Polytechnique Federale de Lausanne EPFL-BCH, Lausanne, CH-1015, Switz.
SOURCE: Chimia (2005), 59(3), 81-84
CODEN: CHIMAD; ISSN: 0009-4293
PUBLISHER: Swiss Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Ru(II) and Os(II) p-cymene dichloride complexes with either a pta (1,3,5-triaza-7-phosphatricyclo[3.3.1.1]decane) or [pta-Me]Cl ligand which exhibit anticancer activity were prepared and characterized by 1H and 31P NMR spectroscopy and mass spectrometry. Three of the complexes, viz. [Os(η6- p-cymene)Cl2(pta)] and [M(η6- p-cymene)Cl2(pta-Me)]Cl (M = Ru, Os), also were characterized by single-crystal x-ray diffraction. The pta complexes are selective anticancer agents, whereas the pta-Me+ complexes are indiscriminate and damage both cancer and healthy cells but represent models for the protonated pta adduct which was implicated in drug activity. To establish a link between their biol. activity and the effect they have on DNA (a likely in vivo target), the reactivity of the complexes toward a 14-mer oligonucleotide (5'-ATACATGGTACATA-3') was

studied using electrospray ionization mass spectrometry. The complexes bind to the oligonucleotide with loss of chloride and in some cases loss of the arene. Loss of arene appears to be most facile with the Ru-pta complexes but also takes place with the Ru-pta-Me complexes, whereas arene loss is not observed for the Os complexes. As pH is reduced, increased binding to the oligonucleotide is observed, as evidenced from mass spectrometric relative intensities. Binding energies between the metal centers and the surrounding ligands were calculated using d. functional theory (DFT). The calculated energies rationalize the exptl. observed tendencies for arene loss and show that the pta ligands are relatively strongly bound. Exchange of metal center (Ru vs. Os), methylation or protonation of the pta ligand, or change of the arene (p-cymene vs. benzene) results in significant differences in the metal-arene binding energies while leaving the metal-phosphine bond strength essentially unchanged. Significantly lower binding energies and reduced hapticity are predicted for the exchange of arene by nucleobases. The latter show higher binding energies for N σ-bonding than for π-bonding.

ACCESSION NUMBER: 2005:248426 CAPLUS
DOCUMENT NUMBER: 143:7797
TITLE: Binding of Organometallic Ruthenium(II) and Osmium(II) Complexes to an Oligonucleotide: A Combined Mass Spectrometric and Theoretical Study
AUTHOR(S): Dorcier, Antoine; Dyson, Paul J.; Gossens, Christian; Rothlisberger, Ursula; Scopelliti, Rosario; Tavernelli, Ivano
CORPORATE SOURCE: Institut des Sciences et Ingenierie Chimiques, Ecole Polytechnique Federale de Lausanne (EPFL), Lausanne, CH-1015, Switz.
SOURCE: Organometallics (2005), 24(9), 2114-2123
CODEN: ORGND7; ISSN: 0276-7333
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:7797
REFERENCE COUNT: 94 THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB We analyzed DNA duplexes modified at central guanine residues by monofunctional Ru(II) arene complexes [(η6-arene)Ru(II)(en)(Cl)]+ (arene = tetrahydroanthracene or p-cymene, Ru-THA or Ru-CYM, resp.). These two complexes were chosen as representatives of two different classes of Ru(II) arene compds. for which initial studies revealed different binding modes: one that may involve DNA intercalation (tricyclic-ring Ru-THA) and the other (mono-ring Ru-CYM) that may not. Ru-THA is .apprx.20 times more toxic to cancer cells than Ru-CYM. The adducts of Ru-THA and Ru-CYM have contrasting effects on the conformation, thermodn. stability, and polymerization of DNA in vitro. In addition, the adducts of Ru-CYM are removed from DNA more efficiently than those of Ru-THA. Interestingly, the mammalian nucleotide excision repair system has low efficiency for excision of ruthenium adducts compared to cisplatin intra-strand crosslinks.

ACCESSION NUMBER: 2005:63663 CAPLUS
DOCUMENT NUMBER: 143:300867
TITLE: Conformation of DNA Modified by Monofunctional Ru(II) Arene Complexes: Recognition by DNA Binding Proteins and Repair. Relationship to Cytotoxicity
AUTHOR(S): Novakova, Olga; Kasparkova, Jana; Bursova, Vendula; Hofr, Ctirad; Vojtiskova, Marie; Chen, Haimei; Sadler, Peter J.; Brabec, Viktor
CORPORATE SOURCE: Institute of Biophysics, Academy of Sciences of the Czech Republic, Brno, CZ-61265, Czech Rep.
SOURCE: Chemistry & Biology (2005), 12(1), 121-129
CODEN: CBOLE2; ISSN: 1074-5521

PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB The chelating ligand XY in RuII anticancer complexes [Ru(η6-arene)(XY)Cl]n+ has a major influence on the rate and extent of aquation, the pKa of the aqua adduct, and the rate and selectivity of binding to nucleobases. Replacement of neutral ethylenediamine (en) by anionic acetylacetonate (acac) as the chelating ligand increases the rate and extent of hydrolysis, the pKa of the aqua complex (from 8.25 to 9.41 for arene = p-cymene), and changes the nucleobase specificity. For the complexes containing the H-bond donor en, there is exclusive binding to N7 of guanine in competitive nucleobase reactions, and in the absence of guanine, binding to cytosine or thymine but not to adenine. In contrast, when XY is the H-bond acceptor acac, the overall affinity for adenosine (N7 and N1 binding) is comparable to that for guanosine, but there is little binding to cytidine or thymidine.
ACCESSION NUMBER: 2004:900041 CAPLUS
DOCUMENT NUMBER: 142:38379
TITLE: Use of chelating ligands to tune the reactive site of half-sandwich ruthenium(II)-arene anticancer complexes
AUTHOR(S): Fernandez, Rafael; Melchart, Michael; Habtemariam, Abraha; Parsons, Simon; Sadler, Peter J.
CORPORATE SOURCE: School of Chemistry, University of Edinburgh, Edinburgh, EH9 3 JJ, UK
SOURCE: Chemistry--A European Journal (2004), 10(20), 5173-5179
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:38379
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
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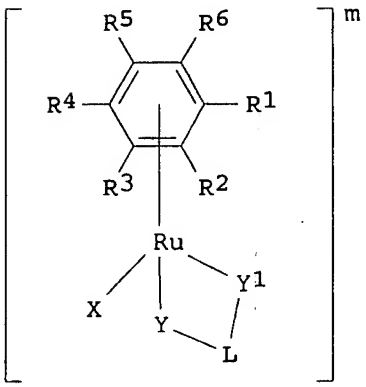

I

AB The preparation of half-sandwich ruthenium(II) compds. I (R1-R6 =

independent to each other H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, hydroxy(C1-6)alkyl, amino(C1-6)alkyl, halo, alkoxycarbonyl, aminocarbonyl, SO3H, aminosulfonyl, aryloxy, C1-6 alkoxy, C1-6 alkylthio, etc.; X = O-, N-, S- donor ligand, halo, etc.; Y-L-Y1 = bidentate ligand bearing neg. charge, etc.; m = -1, 0, 1), useful in the treatment and/or prevention of cancer, is described. Thus, reaction of [(η6- p-cymene)RuCl2]2 with sodium acetylacetonate monohydrate in Me2CO gave 59% title compound, [(η6- p-cymene)RuCl(H3CCOCHCOCH3-O,O)].

ACCESSION NUMBER: 2004:41485 CAPLUS
DOCUMENT NUMBER: 140:94145
TITLE: Preparation of half-sandwich ruthenium anticancer complexes
INVENTOR(S): Sadler, Peter John; Fernandez Lainez, Rafael; Habtemariam, Abraba; Melchart, Michael; Jodrell, Duncan Ian
PATENT ASSIGNEE(S): The University Court, the University of Edinburgh, UK
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004005304	A1	20040115	WO 2003-GB2879		20030704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2491640	A1	20040115	CA 2003-2491640		20030704
AU 2003251159	A1	20040123	AU 2003-251159		20030704
BR 2003012470	A	20050426	BR 2003-12470		20030704
EP 1558620	A1	20050803	EP 2003-762788		20030704
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1665826	A	20050907	CN 2003-816000		20030704
JP 2005536487	T	20051202	JP 2004-518958		20030704
NO 2005000640	A	20050322	NO 2005-640		20050204
US 2006058270	A1	20060316	US 2005-520239		20050718
PRIORITY APPLN. INFO.:			GB 2002-15526	A	20020705
			WO 2003-GB2879	W	20030704

OTHER SOURCE(S): CASREACT 140:94145; MARPAT 140:94145
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Modifications of natural DNA in a cell-free medium by antitumor monodentate Ru(II) arene compds. of the general formula [(η6-arene)Ru(en)Cl]+ (arene = biphenyl, dihydroanthracene, tetrahydroanthracene, p-cymene, or benzene; en = ethylenediamine) were studied by atomic absorption, melting behavior, transcription mapping, circular and linear dichroism, plasmid unwinding, competitive ethidium displacement, and differential pulse polarog. The results indicate that these complexes bind preferentially to guanine residues in double-helical DNA. The data are consistent with DNA binding of the complexes containing biphenyl, dihydroanthracene, or tetrahydroanthracene ligands that involves combined coordination to G N7

and noncovalent, hydrophobic interactions between the arene ligand and DNA, which may include arene intercalation and minor groove binding. In contrast, the single hydrocarbon rings in the p-cymene and benzene ruthenium complexes cannot interact with double-helical DNA by intercalation. Interestingly, the adducts of the complex containing p-cymene ligand, which has Me and iso-Pr substituents, distort the conformation and thermally destabilize double-helical DNA distinctly more than the adducts of the three multiring ruthenium arene compds. It has been suggested that the different character of conformational alterations induced in DNA, and the resulting thermal destabilization, may affect differently further "downstream" effects of damaged DNA and consequently may result in different biol. effects of this new class of metal-based antitumor compds. The results point to a unique profile of DNA binding for Ru(II) arene compds., suggesting that a search for new anticancer compds. based on this class of complexes may also lead to an altered profile of biol. activity in comparison with that of metal-based antitumor drugs already used in the clinic or currently on clin. trials.

ACCESSION NUMBER: 2003:726446 CAPLUS
DOCUMENT NUMBER: 139:345326
TITLE: DNA Interactions of Monofunctional Organometallic Ruthenium(II) Antitumor Complexes in Cell-free Media
AUTHOR(S): Novakova, Olga; Chen, Haimei; Vrana, Oldrich; Rodger, Alison; Sadler, Peter J.; Brabec, Viktor
CORPORATE SOURCE: Institute of Biophysics, Academy of Sciences of the Czech Republic, Brno, CZ-61265, Czech Rep.
SOURCE: Biochemistry (2003), 42(39), 11544-11554
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Two diruthenium(II) complexes [RuCl2(p-cymene)]2(μ-BESE), (1), [RuCl2(p-cymene)]2(μ-BESP) (2), and mononuclear [RuCl(p-cymene)(BESE)]PF6 (3), containing the disulfoxides BESE and BESP, were synthesized and characterized by elemental anal., and NMR and IR spectroscopies, and contain S-bound sulfoxide groups; the disulfoxides are EtS(O)(CH2)nS(O)Et, where n = 2 (BESE) or 3 (BESP). Complexes 1 and 3 were also characterized by x-ray crystallog. Preliminary in vitro tests of 1 and 3 were conducted using the MTT assay, which measures mitochondrial dehydrogenase activity as an indication of cell viability. These complexes showed in vitro anti-cancer activity against a human mammary cancer cell line (MDA-MB-435s) with IC50 values of 360 and 55 μM, resp.

ACCESSION NUMBER: 2003:576969 CAPLUS
DOCUMENT NUMBER: 140:181590
TITLE: The synthesis, structural characterization, and in vitro anti-cancer activity of chloro(p-cymene) complexes of ruthenium(II) containing a disulfoxide ligand
AUTHOR(S): Huxham, Lynsey A.; Cheu, Elizabeth L. S.; Patrick, Brian O.; James, Brian R.
CORPORATE SOURCE: Department of Chemistry, University of British Columbia, Vancouver, BC, V6T 1Z1, Can.
SOURCE: Inorganica Chimica Acta (2003), 352, 238-246
CODEN: ICHAA3; ISSN: 0020-1693
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:181590
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

AB The recognition of nucleic acid derivs. by organometallic ruthenium(II) arene anticancer complexes of the type [(η6-arene)Ru(II)(en)X] (en = ethylenediamine, arene = biphenyl (Bip), tetrahydroanthracene (THA), dihydroanthracene (DHA), p-cymene (Cym) or benzene (Ben), X = Cl- or H2O) was studied using 1H, 31P and 15N (15N-en) NMR spectroscopy. For mononucleosides, [(η6-Bip)Ru(en)]2+ binds only to N7 of guanosine, to N7 and N1 of inosine, and to N3 of thymidine. Binding to N3 of cytidine was weak, and almost no binding to adenosine was observed The reactivity of the various binding sites of nucleobases toward Ru at neutral pH decreased in the order G(N7) > I(N7) > I(N1), T(N3) > C(N3) > A(N7), A(N1). Therefore, pseudo-octahedral diamino Ru(II) arene complexes are much more highly discriminatory between G and A bases than square-planar Pt(II) complexes. Such site-selectivity appears to be controlled by the en NH2 groups, which H-bond with exocyclic oxygens but are nonbonding and repulsive toward exocyclic amino groups of the nucleobases. For reactions with mononucleotides, the same pattern of site selectivity was observed, but, in addition, significant amts. of the 5'-phosphate-bound species (40-60%) were present at equilibrium for 5'-TMP, 5'-CMP and 5'-AMP. In contrast, no binding to the phosphodiester groups of 3', 5'-cyclic-GMP (cGMP) or cAMP was detected. Reactions with nucleotides proceeded via aquation of [(η6-arene)Ru(en)Cl]+, followed by rapid binding to the 5'-phosphate, and then rearrangement to give N7, N1, or N3-bound products. Small amts. of the dinuclear species, e.g., Ru-O(PO3)GMPN7-Ru, Ru-O(PO3)IMPN1-Ru, Ru-O(PO3)TMPN3-Ru, Ru-N7IMPN1-Ru, and Ru-N7InoN1-Ru were also detected. In competitive binding expts. for [(η6-Bip)Ru(en)Cl]+ with 5'-GMP vs. 5'-AMP or 5'-CMP or 5'-TMP, the only final adduct was [(η6-Bip)Ru(en)(N7-GMP)]. Ru-H2O species were more reactive than Ru-OH species. The presence of Cl- or phosphate in neutral solution significantly decreased the rates of Ru-N7 binding through competitive coordination to Ru. In kinetic studies (pH 7.0, 298 K, 100 mM NaClO4), the rates of reaction of cGMP with {(η6-arene)Ru(II)(en)X}n+ (X = Cl- or H2O) decreased in the order: THA > Bip > DHA >> Cym > Ben, suggesting that N7-binding is promoted by favorable arene-purine hydrophobic interactions in the associative transition state. These findings have revealed that the diamine NH2 groups, the hydrophobic arene, and the chloride leaving group have important roles in the novel mechanism of recognition of nucleic acids by Ru arene complexes, and will aid the design of more effective anticancer complexes, as well as new site-specific DNA reagents.

ACCESSION NUMBER: 2002:894426 CAPLUS
DOCUMENT NUMBER: 138:106822
TITLE: Highly Selective Binding of Organometallic Ruthenium Ethylenediamine Complexes to Nucleic Acids: Novel Recognition Mechanisms
AUTHOR(S): Chen, Haimei; Parkinson, John A.; Morris, Robert E.; Sadler, Peter J.
CORPORATE SOURCE: Department of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: Journal of the American Chemical Society (2003), 125(1), 173-186
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:106822
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

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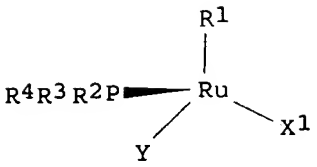

I

AB The preparation of title compds. I (R1 = arene; R2, R3, R4 = same or different, C1-6 alkyl, (un)substituted aryl, R2, R3, and R4 may together with the phosphorous atom form a cycloalkyl group, such group being optionally heterocyclic; Y = halo, SCN, organophosphino, etc.; X1 = halo, SCN, and a dimer thereof, etc.), useful in cancer therapy, is described. Thus, reaction of [Ru(p-cymene)Cl2]2 (preparation given) with 1,3,5-triaza-7-phosphaadamantane (preparation given) in MeOH for 3 H gave title compound, p-cymene-ruthenium(II) 1,3,5-triaza-7-phosphaadamantane dichloride. The biol. activity of the compds. prepared is given.

ACCESSION NUMBER: 2002:391727 CAPLUS
DOCUMENT NUMBER: 136:386263
TITLE: Ruthenium-aryl-compounds in cancer therapy
INVENTOR(S): Dyson, Paul
PATENT ASSIGNEE(S): University of York, UK
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040494	A1	20020523	WO 2001-GB5047	20011116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002015111	A5	20020527	AU 2002-15111	20011116
PRIORITY APPLN. INFO.:			GB 2000-28025 A	20001117
			WO 2001-GB5047 W	20011116

OTHER SOURCE(S): MARPAT 136:386263
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB Inhibition of the growth of the human ovarian cancer cell line A2780 by organometallic ruthenium(II) complexes of the type [(η6-arene)Ru(X)(Y)(Z)], where arene is benzene or substituted benzene, X, Y, and Z are halide, acetonitrile, or isonicotinamide, or X,Y is ethylenediamine (en) or N-ethylethylenediamine, has been investigated. The x-ray crystal structures of the complexes [(η6- p-cymene)Ru(en)Cl]PF6 (I), [(η6- p-cymene)RuCl2(isonicotinamide)], and [(η6-biphenyl)Ru(en)Cl]PF6 are reported. They have "piano stool" geometries with η6 coordination of the arene ligand. Complexes with X,Y as a chelated en ligand and Z as a monofunctional leaving group had the highest activity. Some complexes were as active as carboplatin. Hydrolysis of the reactive Ru-Cl bond in I

was detected by HPLC but was suppressed by the addition of chloride ions. I binds strongly and selectively to G bases on DNA oligonucleotides to form monofunctional adducts. No inhibition of topoisomerase I or II by complex I was detected. These chelated Ru(II) arene complexes have potential as novel metal-based anticancer agents with a mechanism of action different from that of the Ru(III) complex currently on clin. trial.

ACCESSION NUMBER: 2001:719202 CAPLUS
DOCUMENT NUMBER: 136:15044
TITLE: Inhibition of Cancer Cell Growth by Ruthenium (II) Arene Complexes
AUTHOR(S): Morris, Robert E.; Aird, Rhona E.; Murdoch, Piedad del Socorro; Chen, Haimei; Cummings, Jeff; Hughes, Nathan D.; Parsons, Simon; Parkin, Andrew; Boyd, Gary; Jodrell, Duncan I.; Sadler, Peter J.
CORPORATE SOURCE: Department of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK
SOURCE: Journal of Medicinal Chemistry (2001), 44(22), 3616-3621
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
AB The water soluble complex [Ru(η6- p-cymene)Cl2(pta)] (pta = 1,3,5-triaza-7-phosphatricyclo[3.3.1.1]decane), exhibits pH dependent DNA damage; the pH at which damage is greatest correlates well to the pH environment of cancer cells.

ACCESSION NUMBER: 2001:528379 CAPLUS
DOCUMENT NUMBER: 135:352415
TITLE: [Ru(η6- p-cymene)Cl2(pta)] (pta = 1,3,5-triaza-7-phosphatricyclo[3.3.1.1]decane): a water soluble compound that exhibits pH dependent DNA binding providing selectivity for diseased cells
AUTHOR(S): Allardyce, Claire S.; Dyson, Paul J.; Ellis, David J.; Heath, Sarah L.
CORPORATE SOURCE: Department of Chemistry, The University of York, Heslington, York, YO10 5DD, UK
SOURCE: Chemical Communications (Cambridge, United Kingdom) (2001), (15), 1396-1397
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
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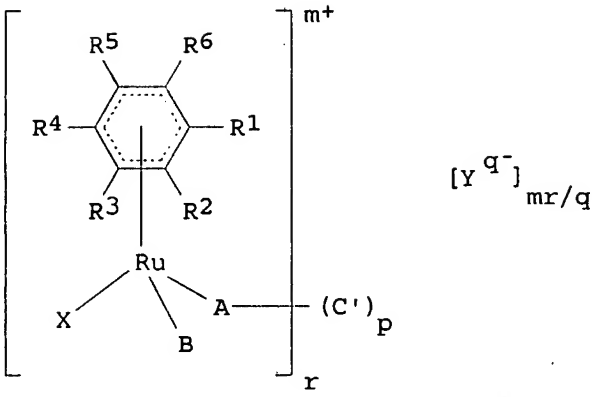

I

AB Title compds. I (R1, R2, R3, R4, R5, R6 = H, alkyl, -CO2R', aryl, alkylaryl, which latter two groups are optionally substituted on the aromatic ring; R' = alkyl, aryl, alkaryl; X = halo, H2O, (R')(R'')SO, R'CO2-, (R')(R'')C:O, R'' = alkyl, aryl, alkaryl; Y = counterion; m = 0-1; q = 1-3; C' = C1-12 alkylene, optionally substituted in or on the alkylene chain, bound to two A groups; p = 0-1 and r = 1 when p is 0 and r is 2 when p is 1; and A and B are: each independently N-donor nitrile ligands; or B is halo and A is an N-donor pyridine ligand, optionally substituted at one or more of the carbon atoms of the pyridine ring; or p is 0, A is NR7R8 and B is NR9R10, wherein R7, R8, R9 and R10 independently represent H or alkyl, and A and B are linked by an alkylene chain, optionally substituted in or on the alkylene chain; or p is 1, A is NR7 and B is NR9R10, wherein R7, R9 and R10 are as previously defined, and A and B are linked by an alkylene chain, optionally substituted) were prepared which may be used in the treatment and/or prevention of cancer.

ACCESSION NUMBER: 2001:319903 CAPLUS
DOCUMENT NUMBER: 134:326632

TITLE: Half-sandwich ruthenium(II) compounds comprising nitrogen containing ligands for treatment of cancer

INVENTOR(S): Morris, Robert Edward; Sadler, Peter John; Chen, Haimei; Jodrell, Duncan
PATENT ASSIGNEE(S): The University Court, the University of Edinburgh, UK

SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030790	A1	20010503	WO 2000-GB4144	20001026
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1224192	A1	20020724	EP 2000-971599	20001026
EP 1224192	B1	20050831		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
JP 2003512471	T	20030402	JP 2001-533142	20001026
AT 303393	T	20050915	AT 2000-971599	20001026
ES 2248136	T3	20060316	ES 2000-971599	20001026
US 2003023088	A1	20030130	US 2002-134404	20020426